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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/756,768	01/14/2004	Samuel Chun-Lap Lo	P69448US0	1516

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EXAMINER	
SAUNDERS, DAVID A	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 09/15/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/756,768	LO ET AL.	
	Examiner	Art Unit	
	David A. Saunders, PhD	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-9 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-9 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Claims 1-9 are pending and under examination.

The drawings are NOT objected to because they have been printed in applicant's PG publication US 2005/0153367 and are thus printable in any granted US patent. In the event that applicant intends to submit full tone photographs/photocopies of the 2D gels, it is applicant's responsibility to do so.

Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d).

The disclosure is objected to because of the following informalities:
At page 3, line 31 "splen cytes" should read as –splenocytes--.
At page 6, line 1 "biotinated" should read as –biotinylated--.
Appropriate correction is required.

Claim 1 is objected to because of the following informalities: In claim 1, line 1, it is believed that insertion of –a-- is intended between "detecting" and "working". Appropriate correction is required.

Claims 1-9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 1 "the compound" lacks antecedent basis.

Claim 1 is incomplete because it fails to state any result of the step of "incubating" the viable splenocytes that relates the step to the purpose of "detecting working mechanism".

Claim 5 fails to state whether the "step of analyzing" occurs before or after the "step of incubating".

Claim 6 fails to state the source of the "production" of the recited proteins. Are these produced by the splenocytes?

Claim 6 fails to state whether the "step of detecting" occurs before, after, or simultaneously with the "step of analyzing".

Claims 1-9 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant was not in possession of detecting the "working mechanism" of a substance on an organism. Beyond the addition of a test substance to a culture of splenocytes and detecting global changes in protein expression via 2D PAGE analysis or detecting changes in the expression of particular proteins (e.g. as listed in claim 6), applicant has given the reader no insight as to how these observed changes relate to any "working mechanism" in the organism. Applicant has observed changes in the expression particular proteins recited in claim 6 and has then merely stated what was already known in the art about the mechanistic function/role of such proteins in cellular metabolism/differentiation. See, for example, para.[0054]-[0056] of US 2005/0153367. Applicant has further illustrated these art known functions/roles of these proteins in Fig. 5; however, beyond these conclusions, applicant has offered no new insights into the "working mechanism" of the substance's metabolism/differentiation in splenocytes.

Furthermore, by observing these changes in the expression of the particular proteins, as disclosed and recited in claim 6, of cells in culture, one does not gain a full insight into the "working mechanism of a substance on an organism", since any given substance may affect the cells of organs other than the spleen and may affect cells of types other than the macrophages, B-cells and T-cells found in the spleen.

Claims 1-9 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicant has not enabled the detecting of the "working mechanism" of a substance on an organism. Beyond the addition of a test substance to a culture of splenocytes and detecting global changes in protein expression via 2D PAGE analysis or detecting changes in the expression of particular proteins (e.g. as listed in claim 6), applicant has given the reader no insight as to how to relate these observed changes relate to any "working mechanism" in the organism. Applicant has observed changes in the expression particular proteins recited in claim 6 and has then merely stated what was already known in the art about the mechanistic function/role of such proteins in cellular metabolism/differentiation. See, for example, para.[0054]-[0056] of US 2005/0153367. Applicant has further illustrated these art known functions/roles of these proteins in Fig. 5; however, beyond these conclusions, applicant has given no direction as to how one is to further investigate the "working mechanism" of the substance's metabolism/differentiation in splenocytes.

Furthermore, the observation of these changes in the expression of the particular proteins, as disclosed and recited in claim 6, does not enable one to gain a full insight into the "working mechanism of a substance on an organism", since any given substance may affect the cells of organs other than the spleen

and may affect cells of types other than the macrophages, B-cells and T-cells found in the spleen. The detecting done merely in an in vitro culture of splenocytes merely tells one whether the substance in some way affects the metabolic function of the splenocytes; that is, the claimed test is merely an initial screening test, and one of skill would recognize that in vivo studies would need to be conducted before one could make conclusions about the "working mechanism of a substance on an organism"

It is suggested that applicant claim a --method of drug screening-- in lieu of a "method of detecting the working mechanism of a substance on an organism". Such a method would be supported by para. [0002] and [0017]-[0018] of US 2005/0153367.

Claims 5-6 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant was not in possession of a method of analyzing the incubated "substance" by a method of 2-dimensional polyacrylamide gel electrophoresis" (2D PAGE). To the contrary, applicant's disclosed method of 2D PAGE analyzes the repertoire of proteins produced by the incubated splenocytes, rather than incubated "substance" per se. See para. {0033]-[0041] of applicant's PG publication US 2005/0153367.

Claims 5-6 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicant has not enabled a method of analyzing the incubated "substance" by a method of 2-dimensional polyacrylamide gel electrophoresis" (2D PAGE). Since applicant's disclosed method of 2D PAGE analyzes the repertoire of proteins produced by the incubated splenocytes, rather than the incubated "substance" per se, applicant has given the reader no direction as to how one might analyze the incubated "substance". In fact, since the immunomodulatory substances contemplated by applicant for use in the claimed method would include many substances that are not proteins, the one exemplification of 2D PAGE would not be reasonably expected by one of skill to be applicable for the analysis of incubated substances that are not proteins.

Furthermore, even if the incubated substance were to be a protein, applicant has not shown how to analyze this particular protein per se by 2D PAGE. Applicant has only shown how to conduct 2D PAGE analysis with a whole incubated cell lysate, which includes all of the proteins of the incubated cells. Applicant has not shown how to identify any incubated protein "substance" or any metabolic products thereof by such 2D PAGE analysis.

Claim 6 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant was not in possession of a method of analyzing the "precursors and/or breakdown products" of the Markush group members recited in claim 6. Applicant has not described these the "precursors and/or breakdown products" such that one would be able to envision which "precursors and/or breakdown products" have any relationship to "detecting working mechanism" as required by base claim 1. The only protein products that can be detected by 2D PAGE (as required by base claim 5) and that applicant has pointed out as having any relationship to "detecting working mechanism" are those listed as the Markush

Group members per se. Applicant has not pointed out where any of these "precursors and/or breakdown products" might be found on the 2D PAGE pattern; and, since applicant has not identified the molecular weights and charge characteristics of any of the "precursors and/or breakdown products" one of skill would not be able to envision where these "precursors and/or breakdown products" might be found on a 2D PAGE pattern. The particular Markush group members recited in claim 6 are thus not representative of the genus of protein products encompassed by claim 6.

Claim 6 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicant has not enabled of a method of analyzing the "precursors and/or breakdown products" of the Markush group members recited in claim 6. Applicant has not described these the "precursors and/or breakdown products" such that one would be able to detect those which have any relationship to "detecting working mechanism" as required by base claim 1. The only protein products that applicant has shown to be detected by 2D PAGE (as required by base claim 5) and that applicant has pointed out as having any relationship to "detecting working mechanism" are those listed as the Markush Group members per se. Applicant has not directed the reader to as to where any of these "precursors and/or breakdown products" might be found on the 2D PAGE pattern. Since applicant has not identified the molecular weights and charge characteristics of any of the "precursors and/or breakdown products" one of skill would be required to conduct undue experimentation in order to find out where any of these "precursors and/or breakdown products" might be found on a 2D PAGE pattern.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-2, 5 and 9 are rejected under 35 U.S.C. 102(a) or (b) as being anticipated by Wang et al (Ref AC on 1449).

The reference has an author who is not an inventor and is thus cited under 102. Since the publication date during 2003 cannot be determined the rejection is made alternatively under 102 (a) or (b). If 102 (a) applies, then applicant may overcome with the filling of a Rule 1.132 declaration in accord with In re Katz 214 USPQ 15.

Wang et al teach 2D PAGE analysis of the comparative protein expression patterns in control and in substance/drug (i.e. Lipopolysaccharide or Con A) treated splenocytes from rats. See Fig 1. Such is consistent with instant claims 1-2 and 5 (at least to the extent that the examiner can understand applicant's described embodiment of claim 5). The phrase "detecting working mechanism" in claim 1 is considered met by the teachings that the method is "to analyze changes in protein expression" (p 580, col. 1). Applicant has given no definition of what the phrase "detecting working mechanism" is intended to encompass; it is thus proper for the examiner to broadly interpret this as encompassing a method which is conducted "to analyze changes in protein expression". If applicant considers that the phrase "detecting working mechanism" corresponds to applicant's disclosure of identifying the protein spots of the gel that undergo some sort of change in response to the substance/drug in relation some sort of database which would tell one just what protein these spots represent, then no

weight is given to this phrase, since it refers to a mere mental step, rather than to any chemical analysis method step.

Regarding claim 9, Wang et al do not show any immune response to an antigenic substance. However, Lipopolysaccharide or Con A modulate the activity of immune cells among the splenocytes. Since applicant's one exemplification in the disclosure of an "immune response" is that in which ginseng modulates the activity of immune cells among the splenocytes, it is proper for the examiner to likewise reject claim 9.

Claims 1-4 and 7-9 are rejected under 35 U.S.C. 102(b) as being anticipated by Liu et al (ref AJ cited on 1449) in light of Moore et al (JAMA 199, 519, 1967).

Liu et al teach analysis of IL-2 mRNA production and of IL-2 protein in rat splenocytes in response to Ginsenoside Rg1 vs. controls. From these results, Liu et al consider that Rg1 is an immunoregulator. See Abstract and Tab 1. This showing and conclusion drawn therefrom are sufficient to anticipate claims 1-2.

Regarding claims 3-4, there is an apparent teaching of culturing at 37 degrees C (page 819, third para., line 2).

Regarding claims 7-8, there is an apparent teaching of culturing in RPMI-1640 medium (page 819, third para., line 2). RPMI-1640 medium has a pH of 7.2; see Moore et al at page 519, col. 2. Thus Liu et al inherently cultured cells "at a pH of about 7."

Regarding claim 9, any showing that a substance modulates the activity of immune cells among the splenocytes, is properly considered as anticipating.

Claims 1, 3-4 and 7-9 are rejected under 35 U.S.C. 102(b) as being anticipated by Gao et al (ref AA cited on 1449) in light of Moore et al.

Gao et al teach analysis of interferon-gamma production in mouse splenocytes in response to polysaccharides from ginsen vs. controls. From these results, Gao et al consider that polysaccharides PF3111 and PGBA12 are

immunostimulating agents. See Abstract and para spanning pages 11-99-1200. This showing and conclusion drawn therefrom are sufficient to anticipate claim 1.

Regarding claims 2-3, there is a teaching of culturing at 37 degrees C (page 1197, col. 2, third full para.).

Regarding claims 7-8, there is a teaching of culturing in RPMI-1640 medium (page 1197, col. 2, third full para.). RPMI-1640 medium has a pH of 7.2; see Moore et al at page 519, col. 2. Thus Gao et al inherently cultured cells "at a pH of about 7."

Regarding claim 9, any showing that a substance modulates the activity of immune cells among the splenocytes, is properly considered as anticipating.

Claims 1-4 and 7-9 are rejected under 35 U.S.C. 102(b) as being anticipated by Siegel et al (6,495,347) in light of Moore et al.

Seigel et al teach methods of culturing naïve lymphocytes with a fusion protein, in order to determine if the fusion protein stimulates a Th1 type immune response. See col. 1, line 45-col. 3, line 44 and col. 12, line 50-col. 13, line 35, for example. The determining of a Th1 type response is consistent with "detecting working mechanism". Siegel et al teach use of spleen cells (col. 2, lines 24-25 and claim 14). Hence instant claims 1-2 and 9 are anticipated.

Regarding claim 2, note teaching of rat at col. 12, line 52.

Regarding claims 3-4 and 7-8, note teachings of culture media and temperature of incubation in Examples 17-21. These are consistent with a pH of about 7 and a temperature of 37 degrees. The RPMI-1640 medium has inherently has a pH of 7.2; see Moore et al at page 519, col. 2.

Claims 1, 3-4 and 7-9 are rejected under 35 U.S.C. 102(b) as being anticipated by Mond et al (5,932,427) in light of Moore et al.

Mond et al teach methods of culturing naïve B-lymphocytes with a compound/composition, in order to determine if the compound/composition stimulates antibody secretion. See col. 4, lines 42-50 and col. 12, line 45-col. 13,

line 32, for example. Examples 1-8 use mouse spleen cells (col. 14, lines 8-26). These experiments determine the effects of IL-3, GM-CSF, IL-1 + IL-2, and CDL40 upon antibody secretion. These examples demonstrate mechanistic aspects of the response (e.g. col. 15, lines 60-64; col. 17, lines 10-17 and 53-55; col. 18, lines 23-25) and are thus consistent with "detecting working mechanism". Hence instant claims 1 and 9 are anticipated.

Regarding claims 3-4 and 7-8, note teachings of culture media and temperature of incubation in Example 1. These are consistent with a pH of about 7 and a temperature of 37 degrees. The RPMI-1640 medium has inherently has a pH of 7.2; see Moore et al at page 519, col. 2.

Claim 6 contains limitations allowable over the prior art of record.

Any inquiry concerning this communication from the examiner should be directed to David A. Saunders, PhD whose telephone number is 571-272-0849. The examiner can normally be reached on Mon.-Thu. from 8:00 am to 5:30 pm. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan, can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Typed 9/12/06 DAS

David A Saunders

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PRIMARY EXAMINER
ART UNIT 182

1644